

# Women with Schizophrenia and Related Disorders

Subjects: Allergy

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Sex and age are important factors influencing physical and mental health in schizophrenia.

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## 1. Introduction

Over the last several decades, a significant amount of research has dealt with the study of gender and sex differences in the biological and behavioral expression of disease. Sex and gender have been found to impact the clinical manifestation of many diseases, as well as their epidemiology (prevalence and incidence) and pathophysiology <sup>[1]</sup>.

Cardiology has been in the forefront of investigating and uncovering substantial biological and sociocultural differences between the sexes with respect to clinical manifestations and outcomes of hypertension, acute coronary syndrome, and heart failure, as well as other cardiac disease <sup>[2]</sup>. The World Health Organization now underscores the fact that “gender is a structural determinant of health” and that, globally, women receive less health care than men while bearing more family responsibilities, with the result that health outcomes are poorer in women than in men. An important example is ischemic heart disease. Women seek help later than men; once help is received, the correct diagnosis takes longer to arrive at, and treatment is too often suboptimal <sup>[2]</sup>.

With respect to mental disorders, gender and sex differences have been described in the susceptibility to specific disorders, in their clinical expression, comorbidity, and treatment response <sup>[3]</sup>. Unfortunately, although sex/gender differences are being reported, their importance has not sufficiently influenced the conduct of clinical treatment trials. Neither recruitment nor the analysis of findings has sufficiently taken sex/gender into account. The vast majority of early clinical trials chiefly recruit male participants, a fact that has led to treatment guidelines based, for the most part, on male response <sup>[3]</sup>.

Although results differ and uncertainties remain, in schizophrenia and in first-episode psychoses, studying gender differences has been helpful in illustrating the heterogeneity of psychotic illness <sup>[4]</sup>. Most studies strongly support the findings that men experience an earlier age of psychosis onset and suffer more frequently than women from severe negative symptoms <sup>[4]</sup>. Comorbid substance use disorders (nicotine, cannabis, alcohol, cocaine) have been repeatedly demonstrated to be more prevalent in men than in women, and clinical outcomes to be superior in women, at least over the course of the reproductive years.

When the reproductive years come to an end, the seeming advantage for women wanes. Thus far, however, the effect of menopause on drug efficacy and on side-effects remains understudied <sup>[5]</sup>. A recent narrative review of randomized controlled trials targeting peri- and postmenopausal women with schizophrenia concludes that a decline in estrogen levels at menopause is associated with worsening psychosis outcomes <sup>[6]</sup>. More recently, Szeliga et al. reported that menopause exerts a negative effect on all women, and, in women with schizophrenia, schizoaffective disorder, and bipolar disorder, it negatively impacts the course of disease <sup>[7]</sup>.

Prior to menopause, women with schizophrenia show a more robust antipsychotic response than they do post menopause. Raloxifene, a selective estrogen receptor modulator, combined with antipsychotics has been recommended as a potential adjunctive therapy to improve psychotic and cognitive symptoms in postmenopausal women with schizophrenia and related disorders <sup>[8]</sup>. Of additional importance is the observation that medical comorbidities increase in women at the time of menopause, more so than they do in male age peers. It is possible that prevention of comorbidities at this age could reduce mortality rates in psychotic illness in both men and women. Physical comorbidities and mental symptoms reinforce each other. For instance, Barker <sup>[9]</sup>, comparing the incidence of mental health symptoms in women before and after hysterectomy, found that psychiatric referrals, especially for depression, significantly increased after surgery.

Besides the effect of menopause and comorbidities on gynecologic disease, personality traits may also have an impact. A community survey conducted by Gath and collaborators and targeting women aged 35–59 found that neuroticism, as well as psychiatric morbidity, were strongly associated with dysmenorrhea, premenstrual tension, excessive menstruation, and hot flushes <sup>[9]</sup>. This association could be mediated via a number of routes including the use of psychiatric medications <sup>[10]</sup>.

Both age and the advent of menopause have been shown to affect the somatic and psychological health of women with schizophrenia <sup>[5][6][11]</sup>, which suggests the possibility that gynecological health, influenced by hormonal fluxes, impacts and, in turn, is impacted by, psychiatric health.

## **2. Discussion**

Breast cancer rates in DD have not been studied, but prolactin-inducing antipsychotics, which are reported to raise overall breast cancer risk, are also used in this disorder, albeit for a shorter cumulative time period. Other gynecological comorbidities appear relatively frequent in psychotic conditions <sup>[12]</sup>, but there is no evidence that their rate in these conditions is higher than it is in the general population. Our second question addressed cancer screening and cancer mortality in this population. All studies agree that the rates of breast and cervix screening for cancer are disproportionately low, and the high mortality rate from breast cancer in these women is at least partially attributable to the lack of timely screening <sup>[13][14][15]</sup>. With respect to menopause, there is evidence that its advent is positively correlated with an increase in the incidence of breast cancer in women with psychotic illness and that it is associated with relatively aggressive tumors <sup>[16]</sup>.

The findings of this review lead to a strong recommendation that psychiatrists and gynecologists work together, particularly with respect to breast cancer prevention and treatment in women with psychotic illness. Pettersson et al. have recommended the development of sex/disease specific prevention programs <sup>[17]</sup>. Gynecology–psychiatry partnerships would be ideal for improving health outcomes of women with psychosis.

The role of antipsychotics in increasing the risk of breast cancer in women with psychosis (via hyperprolactinemia or via weight gain) remains somewhat controversial <sup>[18]</sup> and may depend on the specifics of the antipsychotics used. In nationwide register-based data (2006–2013) that recorded all-cause mortality among Swedish patients with schizophrenia aged 16–64 <sup>[19]</sup>, the lowest mortality was seen in patients on second generation depots, particularly monthly paliperidone injections. Depots were associated with an approximately 30% lower risk of death compared to that seen in patients taking oral antipsychotics. While breast cancer rates may be increased by antipsychotics, in general, adherence to antipsychotic regimens, as assured by depot medication, reduces overall mortality.

While rates may not be disproportional, cervical and ovarian cancers and nonmalignant gynecologic disease (PCOS and endometriosis) are potential problems in this population because of shared risk factors. The fact that women with psychosis lag behind other women with respect to engagement in both primary health care and cancer screening is a major mortality risk <sup>[20]</sup> that lends itself to prevention. Specific difficult-to-improve patient factors, such as cognitive problems, social isolation, apathy, and substance abuse, partially explain low screening rates, but provider factors, such as failure to educate, failure to remind, failure to encourage, and failure to link patients with necessary services, can all be reversed.

Importantly, this population of women lacks the social capital to successfully navigate the health system. Symptoms of psychosis such as amotivation interfere with adherence to treatment recommendations, but critical appointments are also missed because of nonexistent social support. In addition, because of an accumulation of prior risk factors, the tumors of women with psychosis appear to be more aggressive than those of other women <sup>[16]</sup>. Surgical care for these women may also not be optimal, perhaps because they are seen as poor candidates for life-saving procedures. End-of-life care of this population also suffers, and for similar reasons. This urgently calls for close collaboration between primary care, psychiatry, gynecology, and oncology.

In line with this idea, Irwin and collaborators <sup>[21]</sup> developed the Bridge intervention for patients with severe mental illness, a program that includes identification of severe mental illness, person-centered care, and a collaborative approach between psychiatry with oncology. Bridge is a feasible and well-accepted care model for patients with psychosis and comorbid cancer.

Because women with psychotic illness have specific health needs that differ according to stage of life, menopause and postmenopause constituting vulnerable stages <sup>[22]</sup>, the gynecology/psychiatry/oncology partnership could also benefit from collaboration with endocrinology.

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